

Table 3-1 Levels of Significant Exposure to 1,3-butadiene - Inhalation

Key to Figure a	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	LOAEL			Reference Chemical Form	Comments					
				NOAEL (ppm)	Less Serious (ppm)	Serious (ppm)							
ACUTE EXPOSURE													
Death													
1	Rat	1 d 4 h/d				129000 (LC50)	Shugaev 1969						
2	Mouse	1 d 2h/d				122000 (LC50)	Shugaev 1969						
3	Rabbit	1 d 23 min/d				250000	Carpenter et al. 1944						
Systemic													
4	Rat	10 d 6 hr/d Gd 6-15	Bd Wt	200 F (decreased maternal body weight gain)		8000 F (45% decreased maternal body weight gain)	Irvine 1981						
Neurological													
5	Human	1 d 6-8 hr/d		8000			Carpenter et al. 1944						
6	Rabbit	1 d 23 min/d				250000 (anesthesia)	Carpenter et al. 1944						
Reproductive													
7	Mouse (B6C3F1)	5 d 6 h/d		1000 M (73% increase in number of abnormal sperm heads)			DOE/NTP 1988a						
8	Mouse CD-1	6 hr/day 5 days		200 M (increased intrauterine death)			DOE/NTP 1988b						

Table 3-1 Levels of Significant Exposure to 1,3-butadiene - Inhalation (continued)

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3. HEALTH EFFECTS

Key to Figure	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	LOAEL			Reference Chemical Form	Comments
				NOAEL (ppm)	Less Serious (ppm)	Serious (ppm)		
Developmental								
9	Rat (Sprague-Dawley)	10 d 6 hr/d Gd 6-15		1000			DOE/NTP 1987a	
10	Rat	10 d 6 hr/d Gd 6-15	200	8000 (decreased fetal growth)			Irvine 1981	
				1000 (major skeletal malformations)				
11	Mouse (CD-1)	10 d 6 hr/d GD 6-15		40 M (decreased fetal BW in males)			DOE/NTP 1987b	
INTERMEDIATE EXPOSURE								
Death								
12	Mouse	14 wk 5 d/wk 6 hr/d			5000 (increased mortality)		NTP 1984	
13	Mouse (B6C3F1)	13-52 wk 6 hr/d 5 d/wk			200 (increased mortality from 40 weeks of exposure)		NTP 1993	

(continued)

Table 3-1 Levels of Significant Exposure to 1,3-butadiene - Inhalation

Key to Figure ^a	Species (Strain)	Exposure/ Duration/ Frequency (Route)	LOAEL				Reference Chemical Form	Comments
			System	NOAEL (ppm)	Less Serious (ppm)	Serious (ppm)		
Systemic								
14	Rat	13 wk 5 d/wk 6 hr/d	Resp	8000			Crouch et al. 1979	
			Cardio	8000				
			Hemato	8000				
			Musc/skel	8000				
			Hepatic	8000				
			Renal	8000				
			Dermal	8000				
15	Mouse	3-24 wk 6 d/wk 6 hr/d	Hemato			1250 M (macrocytic megaloblastic anemia starting at 6 weeks)	Irons et al. 1986a, b	

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(continued)

Key to Figure	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (ppm)	LOAEL		Reference Chemical Form	Comments
					Less Serious (ppm)	Serious (ppm)		
16	Mouse	14 wk 5 d/wk 6 hr/d	Resp	8000			NTP 1984	
			Cardio	8000				
			Gastro	8000				
			Musc/skel	8000				
			Hepatic	8000				
			Renal	8000				
			Dermal	8000				
17	Mouse (B6C3F1)	13-52 wk 6 hr/d 5 d/wk	Resp		2500 M (13% decreased body weight)		NTP 1993	
			Cardio		200 M (alveolar epithelial hyperplasia after 40 weeks)			
			Ocular	200 M	200 M (endothelial hyperplasia after 40 weeks)			
					625 M (Harderian gland hyperplasia after 26 weeks)			

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(continued)

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3. HEALTH EFFECTS

Key to Figure ^a	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (ppm)	LOAEL		Reference Chemical Form	Comments
					Less Serious (ppm)	Serious (ppm)		
18	Mouse (B6C3F1)	40 wk 6 hr/d 5 d/wk	Resp	200 M	625 M (alveolar epithelial hyperplasia)		NTP 1993	
			Cardio	625				
			Gastro	200	625 (forestomach epithelial hyperplasia)			
			Hemato		62.5 M (decreased erythrocyte counts, hemoglobin concentration, and red cell volume)	200 F (macrocytic megaloblastic anemia)		
			Musc/skel	625				
			Hepatic	625 F				
			Bd Wt	625				
Immuno/ Lymphoret								
19	Mouse (B6C3F1)	40 wk 6 hr/d 5 d/wk			625 F (19% reduction in relative thymus weight)		NTP 1993	
20	Mouse	6-24 wk 5 d/wk 6 hr/d		1250	(lymphoid organ histopathology)		Thurmond et al. 1986	
Neurological								
21	Rat	13 wk 5 d/wk 6 hr/d		8000			Crouch et al. 1979	

(continued)

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Key to Figure	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	LOAEL			Reference Chemical Form	Comments
				NOAEL (ppm)	Less Serious (ppm)	Serious (ppm)		
22	Mouse	14 wk 5 d/wk 6 hr/d		8000			NTP 1984	
		Reproductive						
23	Mouse (CD)	10 wk 6 h/d 5 d/wk			12.5 M (increase in late fetal deaths, exencephalies, and skull abnormalities)		Anderson et al. 1996	
24	Mouse (CD)	4 wk 6 h/d 5 d/wk	12.5 M	65 M (increases in early fetal deaths)			Anderson et al. 1998	
25	Mouse (B6C3F1)	40 wk 6 hr/d 5 d/wk	62.5 F		200 F (ovarian atrophy)		NTP 1993	
		Cancer						
26	Mouse (B6C3F1)	13-52 wk 6 hr/d 5 d/wk			200 M (CEL:lymphocytic lymphoma, histiocytic sarcoma, cardiac hemangiosarcoma, alveolar/bronchiolar adenoma/carcinoma, forestomach squamous cell papilloma/carcinoma, hepatocellular adenoma, Harderian gland adenoma/adenocarcinoma; preputial gland carcinoma)	NTP 1993		

Table 3-1 Levels of Significant Exposure to 1,3-butadiene - Inhalation

(continued)

Key to Figure ^a	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (ppm)	LOAEL		Reference Chemical Form	Comments						
					Less Serious (ppm)	Serious (ppm)								
CHRONIC EXPOSURE														
Death														
27	Rat	105-111 wk 5 d/wk 6 hr/d		1000		8000 (increased mortality)	Owen et al. 1987, Owen and Glaister 1990							
28	Mouse	61 wk 5 d/wk 6 hr/d				625 (increased mortality)	NTP 1984							
29	Mouse (B6C3F1)	2 yr 6 hr/d 5 d/wk				20 (increased mortality)	NTP 1993							
Systemic														
30	Rat	105-111 wk 5 d/wk 6 hr/d	Resp	1000	8000 (increased organ weight, metaplasia)		Owen et al. 1987, Owen and Glaister 1990							
			Cardio	8000										
			Gastro	8000										
			Hemato	8000										
			Hepatic	8000										
			Renal	1000		8000 (nephrosis)								
			Dermal	8000										
			Ocular	8000										

(continued)

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Key to Figure	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	NOAEL (ppm)	LOAEL		Reference Chemical Form	Comments
					Less Serious (ppm)	Serious (ppm)		
31	Mouse	61 wk 5 d/wk 6 hr/d	Resp	625		1250 (atrophy of nasal olfactory epithelium)	NTP 1984	
			Cardio		625 (endothelial hyperplasia)			
			Gastro		625 (epithelial hyperplasia)			
			Musc/skel	1250				
			Hepatic		625 (hepatic necrosis)			
			Renal	1250				
32	Mouse (B6C3F1)	2 yr 6 hr/d 5 d/wk	Resp	6.25 M (alveolar epithelial hyperplasia)			NTP 1993	Animal LOAEL and POD for EPA RfC = 6.25 ppm in mice over 2 years. Mice appear more sensitive than humans.
					625 (endothelial hyperplasia)			
					625 F (forestomach epithelial hyperplasia)			
					200 F (forestomach epithelial hyperplasia)			
					Musc/skel	625		
					Hepatic	62.5 (liver necrosis)		
					Bd Wt	625		

Table 3-1 Levels of Significant Exposure to 1,3-butadiene - Inhalation

(continued)

Key to Figure ^a	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	LOAEL			Reference Chemical Form	Comments
				NOAEL (ppm)	Less Serious (ppm)	Serious (ppm)		
33	Mouse (B6C3F1)	65 wk 6 hr/d 5 d/wk	Hemato	200		625 (macrocytic megaloblastic anemia)	NTP 1993	Neurological
			Bd Wt	625				
34	Rat	105-111 wk 5 d/wk 6 hr/d		8000			Owen et al. 1987, Owen and Glaister 1990	Reproductive
35	Mouse	61 wk 5 d/wk 6 hr/d		1250			NTP 1984	
36	Rat	105-111 wk 5 d/wk 6 hr/d		8000			Owen et al. 1987, Owen and Glaister 1990	Only examined histopathology
37	Mouse	61 wk 5 d/wk 6 hr/d			625 (gonadal atrophy)		NTP 1984	3. HEALTH EFFECTS
38	Mouse (B6C3F1)	2 yr 6 hr/d 5 d/wk			6.25 F (ovarian atrophy)		NTP 1993	
39	Mouse (B6C3F1)	65 wk 6 hr/d 5 d/wk		20 F		62.5 F (ovarian atrophy)	NTP 1993	

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Table 3-1 Levels of Significant Exposure to 1,3-butadiene - Inhalation

(continued)

Key to Figure ^a	Species (Strain)	Exposure/ Duration/ Frequency (Route)	System	LOAEL			Reference Chemical Form	Comments
				NOAEL (ppm)	Less Serious (ppm)	Serious (ppm)		
Cancer								
40	Rat	105-111 wk 5 d/wk 6 hr/d			1000	(CEL: mammary gland adenoma and sarcoma)	Owen et al. 1987, Owen and Glaister 1990	
41	Mouse	61 wk 5 d/wk 6 hr/d			625	(CEL:alveolar/bronchiolar adenoma or carcinoma, malignant lymphoma, hemangiosarcoma, forestomach squamous cell papilloma or carcinoma, mammary gland carcinoma, ovarian granulosa cell tumor)	NTP 1984	
42	Mouse (B6C3F1)	2 yr 6 hr/d 5 d/wk			6.25 F	(CEL: alveolar/bronchiolar adenoma/carcinoma)	NTP 1993	

a The number corresponds to entries in Figure 3-1.

Bd Wt = body weight; Cardio = cardiovascular; CEL = cancer effect level; d = day(s); F = Female; Gastro = gastrointestinal; Gd = gestational day; Hemato = hematological; hr = hour(s); Immuno/Lymphoret = immunological; LC50 = lethal concentration, 50% kill; LOAEL = lowest-observed-adverse-effect level; M = male; min = minute(s); Musc/skel = musculoskeletal; NOAEL = no-observed-adverse-effect level; Resp = respiratory; wk = week(s); yr = year(s)

Figure 3-1 Levels of Significant Exposure to 1,3-Butadiene - Inhalation

Acute (≤ 14 days)

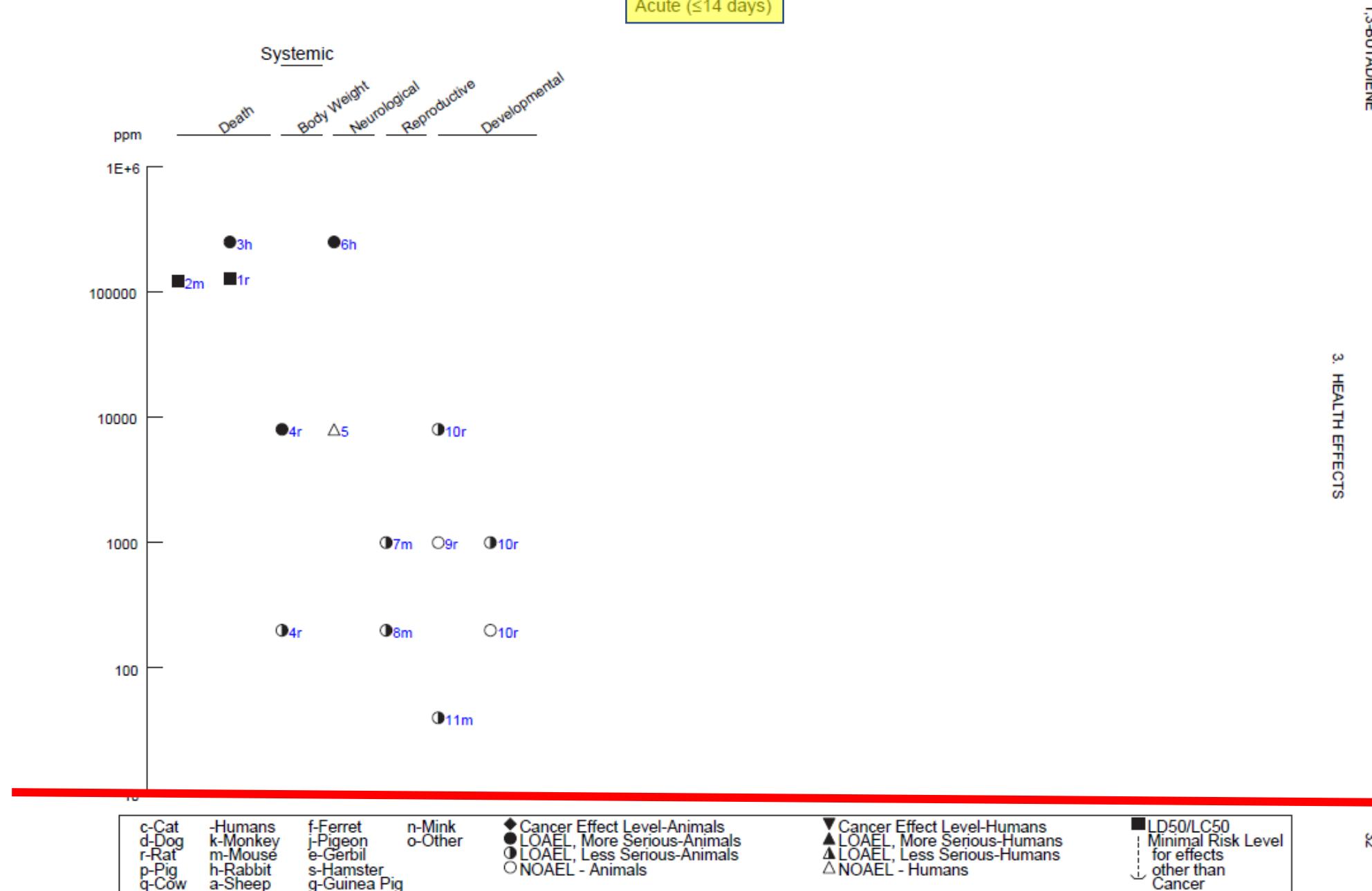


Figure 3-1 Levels of Significant Exposure to 1,3-Butadiene - Inhalation (Continued)

1,3-BUTADIENE

3. HEALTH EFFECTS

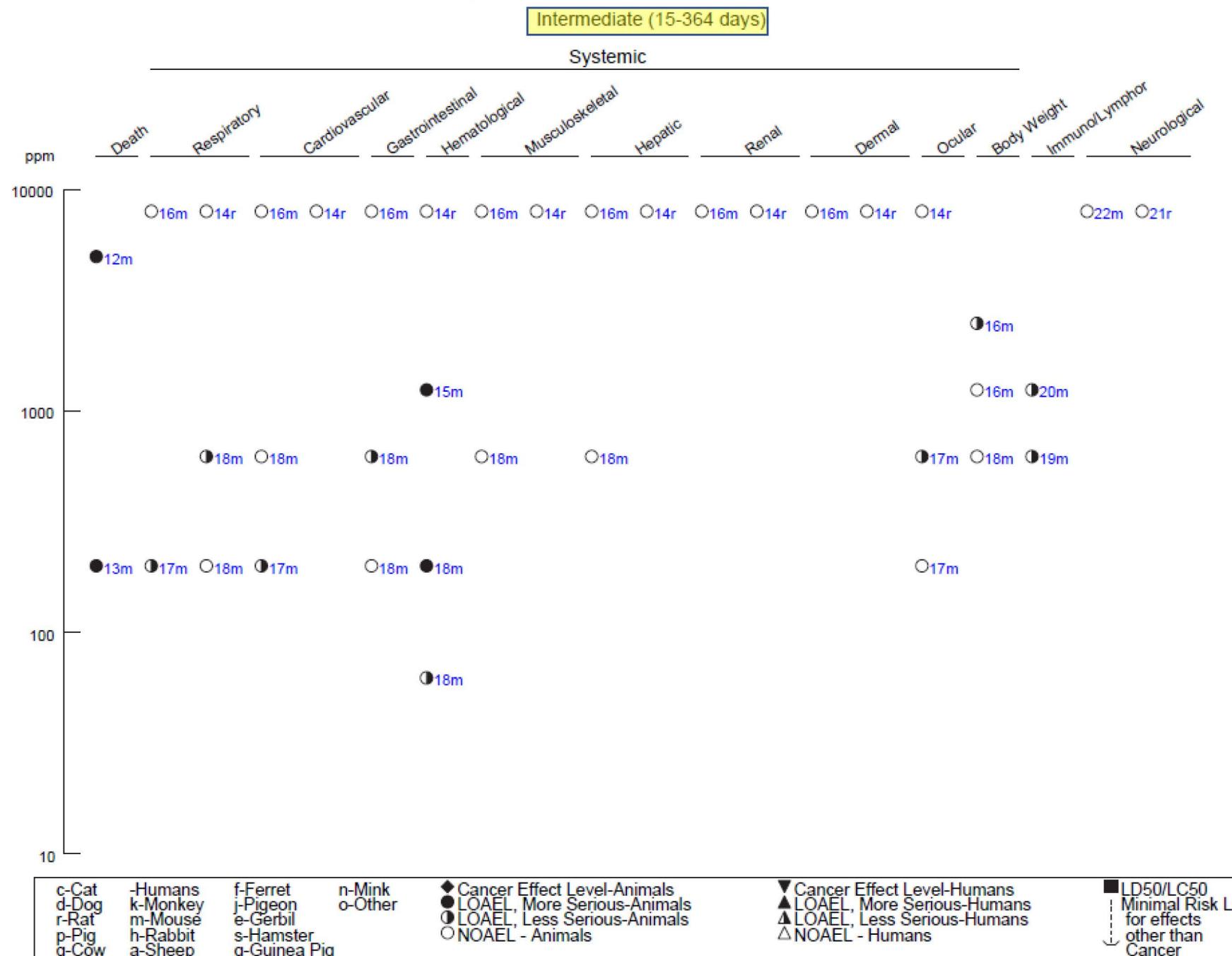
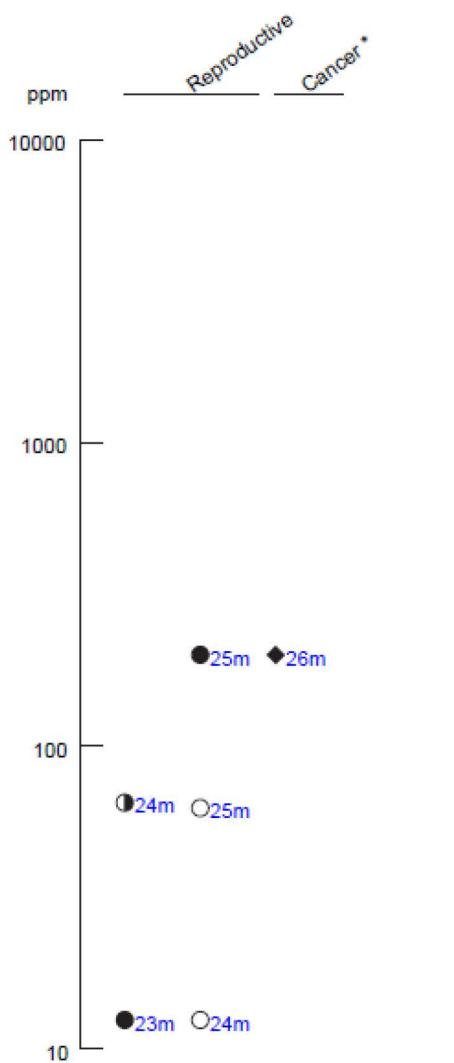


Figure 3-1 Levels of Significant Exposure to 1,3-Butadiene - Inhalation (Continued)

Intermediate (15-364 days)

1,3-BUTADIENE

3. HEALTH EFFECTS



*Doses represent the lowest dose tested per study that produced a tumorigenic response and do not imply the existence of a threshold for the cancer endpoint.

c-Cat	-Humans	f-Ferret	n-Mink	◆ Cancer Effect Level-Animals	▼ Cancer Effect Level-Humans	■ LD50/LC50
d-Dog	k-Monkey	j-Pigeon	o-Other	● LOAEL, More Serious-Animals	▲ LOAEL, More Serious-Humans	Minimal Risk Level
r-Rat	m-Mouse	e-Gerbil		○ LOAEL, Less Serious-Animals	△ LOAEL, Less Serious-Humans	for effects
p-Pig	h-Rabbit	s-Hamster		○ NOAEL - Animals	△ NOAEL - Humans	other than
q-Cow	a-Sheep	g-Guinea Pig				Cancer

Figure 3-1 Levels of Significant Exposure to 1,3-Butadiene - Inhalation (Continued)

